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EXAMINER	
DAHLE, CHUN WU	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/002,211	GOLDENBERG, MILTON D.	
	Examiner	Art Unit	
	CHUN DAHLE	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/30/2007, 12/26/2007, and 02/04/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *78-86 and 93-108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *78-86 and 93-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments, filed on November 30, 2007, December 26, 2007, and February 4, 2008, have been entered.

Claims 1-77 and 87-92 have been previously canceled.

Claims 104-108 have been added.

Claims 78-86 and 93-108 are pending and currently under consideration as they read on the originally elected species of a method of treating immune thrombocytopenic purpura (ITP) and LL2 antibody.

2. This Office Action will be in response to applicant's arguments, filed on November 30, 2007, December 26, 2007, and February 4, 2008.

The rejections of record can be found in the previous Office Action, mailed on August 17, 2006, March 9, 2007, and July 26, 2007.

3. The following references cited on the Foon declaration under 37 C.F.R. 1.132, filed on November 30, 2007 and the Remarks, filed on December 26, 2007 and February 4, 2008, have been listed on PTO-892. Copies of the references are not provided herein.

Knapp et al. Blood. 1989, 74;4:1448-1450.

Schlossman et al. Immunol. Today. 1994, 15;3:98-99.

Nadler et al. J. Clin. Invest. 1981, 67:134-140.

Liu et al. J. Immunol. 1987, 139;10:3521-6. Abstract only.

Schmid et al. American J. of Pathology. 1991, 139;4:701-707.

Shimoyama et al. Japanese Journal of Clinical Oncology. 1983, 13;3:477-488. Abstract only.

Press et al. Blood. 1987. 69;2:584-591.

Press et al. J. Clin. Oncology. 1989. 7;8:1027-38. Abstract only.

Kenneth et al. Blood. 1986. 68;1:1-31.

Dorner et al. Arthritis Research & Therapy. 2006. 8;3:1-11. Pages are renumbered.

Steinfeld et al. Arthritis Research & Therapy. 2006. 8;4:1-11. Pages are renumbered.

Genentech. Updates at Annual Investment Meeting. March 17, 2006.

Wurflein et al. Cancer Research. 1998. 38:3051-3058.

Epstein et al. Cancer Research. 1987. 47:830-840.

Teeling et al. Blood. 2001. 98:1095-1099.

4. In view of applicant's amendment to the claims, the prior rejections under 35 U.S.C. 112, second paragraph against claim 93 regarding the limitation of "an antibody which binds multiple epitopes or antigens" has been withdrawn.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 78-86, 93-101 and newly added claims 104, 105, 107, and 108 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Applicant's arguments in conjunction with the Dorner declaration and the Foon declaration under 37 C.F.R. 1.132 have been fully considered but have not been found persuasive.

The Dorner declaration asserts that at the time of the invention (1992), the term "immune disease" would relate to idiopathic disorders of the immune system. Further, the Dorner declaration argues the instant specification discloses the use of B-cell antibody, the ablation of normal spleen cells, and certain immune disease, such as immune thrombocytopeic purpura (ITP); thus, Dorner asserts that he understood that the disclosure of "antibodies that target the spleen" meant to target immune cells in the spleen. The Dorner declaration appears to argue that

the term "immune disease" is limited to only to disorders such as ITP that belongs to the B-cell hematologic diseases where the immune system is positively regulated, not negatively regulated disorders such as HIV.

The Foon declaration argues that the term "immune disease" is not ambiguous when read in the context of the instant specification and asserts that the most common immune disease are autoimmune disease.

Applicant further argues that the instant application has no indication that the term "immune disease" is defined unusually. Therefore, applicant asserts that the meaning of the "immune disease" would be the plain meaning understood by skilled artisan at the time of the invention (1992). Furthermore, the Foon declaration asserts that the term "immune disease" means autoimmune disease. Thus, applicant argues the term "immune disease" is not indefinite.

This is not found persuasive for following reasons:

In contrast to the assertion by Dorner declaration that "immune disease" is only limited to autoimmune diseases such as ITP, it is noted that the term is not defined by the claims and the instant specification provides no standard for ascertaining the nature or parameters of the "immune disease". The instant claims do not set forth the particular characteristics or specific condition for the "immune disease"; as such the claims fail to particularly point out and distinctly claim the subject matter which the applicant regards as his invention. Further, the specification does not provide any definition for the "immune disease". In response to the Dorner declaration that "immune disease" is only limited to autoimmune disease such as "ITP", it is noted that the instant specification provides no evidence for such interpretation of the term. In fact, the instant specification appears to disclose methods of ablation certain organs and tissues, not only in spleen but also including ablation of T cells (see lines 5-10 in page 7 of the instant specification, or see copy below for applicant's convenience).

> *"(5) ablation of certain normal organs and tissues for other therapeutic purposes, such as the spleen in patients with*

> *immune disease or lymphomas, the bone marrow in patients requiring bone marrow transplantation, or normal cell types involved in pathological processes, such as certain T-lymphocytes in particular immune diseases."*

This strongly suggests that "immune disease" is not merely limited to the scope of autoimmune diseases such as ITP.

In contrast to the Foon declaration that the most common "immune disease" is autoimmune disease, it is noted that the scope of the claims are simply drawn to any "immune disease", not the most common immune disease.

It is noted that expert's opinion on the ultimate legal conclusion must be supported by something more than a conclusory statement. See MPEP 2164.05. In this case, the Dorner and the Foon declarations have not presented necessary evidence to establish that the term is not indefinite at the time of the invention and the declarations also fails to present objective evidence applicable to the full scope of the claims.

It is further noted that affidavits and declaration cannot be used to present disclosure which should have been in the specification as filed. In this case, the Dorner declaration and the Foon declaration cannot be used to define the term "immune disease". Contrary to applicant's argument, nothing in the specification requires that the "immune disease" as claimed to be autoimmune diseases not diseases where the immune system is negatively regulated such as HIV.

While applicant is allowed to claim his invention broadly, he must do so in a way that distinctly identifies the boundaries of his claims. Given that applicant asserts that the term "immune disease" is not given unusual definition (e.g. see page 7 of the Remarks filed on December 26, 2007), the term is interpreted as any disease that affects the immune system; this may include autoimmune diseases such as ITP, but it is not clear how the term can exclude other

immune diseases such as tumors or HIV. Thus, it is unclear whether a person of ordinary skill in the art would have interpreted these claims as only autoimmune diseases such as ITP.

Additionally, in contrast to the assertion of Dorner declaration the term "immune disease" when used in conjunction with B-cell antibody would mean immune diseases such as ITP, it is noted that the Examiner acknowledges that IPT is a species of the immune disease. However, the metes and bounds of genus of "immune disease" is unclear and ambiguous because a skilled artisan could not discern the boundaries of the claim based on the claim language and the specification as well as his or her knowledge of the relevant art.

Therefore, applicant's arguments and the Dorner and Foon declarations have not been found persuasive.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 78-86, 93-103, and newly added claims 104-108 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

The following *written description* rejection is set forth herein.

Claims 78-86, 93103, and newly added claims 104-108 recite "B cell antibody or fragment thereof" as part of the invention.

Applicant's arguments in conjunction with the Dorner declaration and the Foon declaration under 37 C.F.R. 1.132 have been fully considered but have not been found persuasive.

The Foon declaration argues that Knapp et al. and Schlossman et al. teach numerous B cell CD antigens, each corresponds to at least two monoclonal antibodies that identify a particular CD antigen. Thus, applicant asserts that there are numerous monoclonal antibodies to B cell CD antigens were known in the art at the time of the invention.

The Foon declaration argues that Stashenko et al. teach anti-B1 antibody (now anti-CD20 antibody), Nadler et al., Liu et al., US Patent 5,721,108, 6,204,023, 6,652,852, 6,893,625 and WO 88/049386 teach anti-CD20 antibody that recognize CD20 antigen on B cells, and US Patent 5,247,069 teach antibody to Bp50 antigen. The Foon declaration further argues that Press et al. (Blood. 1987. 69;2:584-591) teach method of treating refractory malignant B cell lymphomas using anti-CD20 antibody 1F5; Press et al. (J. Clin. Oncology. 1989. 7;8:1027-38. Abstract only) teach method of treating Non-Hodgkin's lymphoma using anti-CD37 antibody. Furthermore, Foon declaration argues that the genus of the B-cell antibodies share the function of binding B-cell antigen and asserts that the reference Foon et al. teach a list of 30 monoclonal antibodies (to B cell surface antigen) available commercially.

Additionally, Foon asserts that one of skill in the art, upon reading the instant specification would understand that applicant is in possession of a mehtod of the claimed B-cell antibody to treat immune diseases.

This is not found persuasive for following reasons:

While the Examiner acknowledges that Knapp et al. and Schlossman et al. listed several CD antigens that are B cell specific, e.g. CD19, CD20 and CD22, Knapp et al. and Schlossman does not teach any specific antibodies that bind to those B cell specific CD antigens. Further, Knapp et al. teach a variety of CD antigens that are not B cell specific, e.g. CD5 antigen, and are shared by various cells in the immune system such as T cells; however, neither the Foon declaration nor applicant's remark has indicated whether those CD antigens fall within the scope of the B cell antigen.

Further, in contrast to applicant's reliance upon the well-known antibodies recognizing B cell surface markers such as CD 20, it is noted that there is no nexus between the art known monoclonal antibodies and the instant specification and no nexus between the known B cell antibodies and the claimed method of treating an immune disease. It is noted that applicant must convey with reasonable clarity to those skilled in the art that the inventor was in possession of the claimed invention. Furthermore, it is noted that for the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (See Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. MPEP 2163 II.A.3a.ii.

Furthermore, the species of the monoclonal antibodies react with specific B cell markers such as CD20 are not sufficient to support the genus of the claimed B-cell antibody because the genus of the B-cell antibody is extremely large. The term "B-cell antibody" is read as any antibody that binds B cells surface proteins as well as intracellular proteins. In fact, the instant specification discloses that antibodies can be made using antigens isolated from cell membrane

as well as intracellular proteins (e.g. see lines 5-12 on page 11 of the instant specification). Thus, the claimed genus of B-cell antibody is not limited to those that bind B-cell surface proteins such as CD20; rather, B-cell antibody includes any antibody that binds proteins on surface of B-cells as well as those intracellular proteins. As discussed in prior Office Action, it was known in the art at the time of the invention that a mammalian cell may contain up to 30,000 different mRNA sequences that can be translated to proteins as evidenced by the teachings of Sees et al. (EP 0739980, see page 3 in particular). Further as discussed in the previous Office Action mailed on August 17, 2006, Youinou et al. (Autoimmunity Reviews 2006 5:215-221, reference on PTO-892 mailed on August 17, 2006) B-cells express a variety of different cell surface markers depending on the B-cell subsets and locations (e.g. see Table 1 on page 217). Therefore, the genus of the claimed B-cell antibody can contain up to 30,000 different antibodies. Applicant has not provided sufficient evidence to show that there is a known or disclosed correlation or the sufficiently detailed relevant identifying characteristics of the large genus of the claimed "B-cell antibody or fragment thereof". Applicant has not addressed the teachings of Seed et al. and Youinou et al. in her Remarks.

Again, there is insufficient written description of he claimed antibody broadly encompassed by the claimed invention. There is a lack of disclosure of sufficient relevant identifying characteristics coupled with a known or disclosed correlation between function and structure of the broadly diverse antibodies (e.g. antigen specificity) employed in the claimed methods. The claimed methods depend upon finding "B-cell antibody". Without such an antibody, the skilled artisan cannot practice the claimed method of treating an immune disease. It means little to invent a method if one does not have procession of the "B-cell antibody" that is essential to practice the method.

In contrast to the assertion of the Foon declaration that the B cell antibodies have common function of binding B cell surface antigen, it is noted that the fact that antibodies bind B cell surface antigen is not considered relevant identifying characteristics that couple with a known or disclosed correlation between function and structure of the broadly diverse antibodies (e.g. antigen specificity) employed in the claimed methods. Even if all of the genus of B-cell

antibody can be made, not all of the B-cell antibodies can be used in the claimed method of treating an immune disease. It is not clear that which of the monoclonal antibodies that react with human B lymphocytes taught in Table 1 of Kenneth et al. can be used to treat immune disease.

There is insufficient written description of the claimed "B-cell antibody" broadly encompassed by the claimed invention. There is a lack of disclosure of sufficient relevant identifying characteristics coupled with a known or disclosed correlation between function and structure of the broadly diverse antibodies employed in the claimed methods.

Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the genus. That is, the specification provides neither a representative number of species (B-cell antibody or fragments thereof) to describe the claimed genus, nor does it provide a description of structural features that are common to species (B-cell antibody or fragments thereof). The specification provides no structural description of B-cell antibody other than the one specifically exemplified (LL2 antibody); in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed B-cell antibodies looks like. The specification's disclosure is inadequate to describe the claimed genus of B-cell antibodies. Further, there is no described or art-recognized correlation or relationship between the structure of the invention, the B-cell antibody and it's treatment of immune diseases, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of B-cell antibodies which retain the features essential to the instant invention.

Therefore, applicant is not in possession of the claimed method of treating an immune disease by administering a "B cell antibody or fragment" thereof.

Applicant's post filing date evidence submitted to show that certain B-cell antibodies are effective in treating autoimmune disease has been fully considered but have not been found persuasive.

Applicant is reminded the rejection of record is under 35 U.S.C. 112, first paragraph, written description, not enablement. Applicant was not in possession of the claimed method of treating an immune disease by administering the genus of "B-cell antibody" for reasons stated above.

Further, in contrast to applicant's reliance on a method of treating systemic lupus erythematousus or primary SjÖgren's syndrome using anti-CD22 antibody taught by Dorner et al. (Arthritis Res. Ther. 2006. 8;3:pages 1-11 (renumbered)) or Steinfeld et al. (Expert Opin. Biol. Ther. 2006. 6;9:943-9) and method of treating rheumatoid arthritis by companies such as Wyeth and Genentech, it is noted that applicant has not provided any nexus between the prior art diseases systemic lupus erythematousus, primary SjÖgren's syndrome, and rheumatoid arthritis and the instant specification.

Furthermore, the species of anti-CD22 antibody and anti-CD20 antibody are not in commensurate with the scope of the claimed genus of B-cell antibody and the species of systemic lupus erythematousus, primary SjÖgren's syndrome, and rheumatoid arthritis are not in commensurate with the scope of the claimed genus of "an immune disease".

Therefore, applicant's arguments in conjunction with the declarations by Dorner and Foon have not been found persuasive.

9. Claims 93 and 97-100 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

The following *written description* rejection is set forth herein.

Applicant amended the claims on December 26, 2007 so that claims 97-100 became depended upon claim 93. Thus, claims 97-100 have been included in this rejection.

Claims 93 and 97-100 recite "a B-cell antibody or fragment thereof ..... wherein the antibody or fragment thereof is a polyclonal, chimeric or hybrid antibody which binds multiple epitopes or antigens" as part of the invention.

There is insufficient written description in the specification as-filed of the any B-cell antibody or fragment thereof that is a chimeric or hybrid antibody which binds multiple antigens as encompassed in the instant claims.

Applicant's Remarks filed on December 26, 2007 asserts that the amendment has been indicated by the Examiner as a solution to overcome the instant rejection. However, there is no evidence of record that such assurance has been given by the Examiner.

Given that there is insufficient written description in the specification as-filed regarding "B-cell antibody" for reasons discussed above, applicant is not in possession of any B-cell antibody that has additional antigen specificity (e.g. chimeric or hybrid) for reasons set forth in the previous Office Action mailed on July 26, 2007.

Given the absence of additional rebuttal to the outstanding rejection of record in applicant's Remarks, filed on December 26, 2007, the rejection has been maintained for reasons of record.

10. This is a **New Ground of Rejection.** Newly added claims 102 and 105 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The term "B-cell immune disease" recited in claims 102 and 105 is not supported by the original disclosure or claim as filed.

Applicant's amendment, filed February 4, 2008, does not direct to support of the term in the instant specification and does not asserts that no new matter has been added.

However, the specification as filed does not provide sufficient written description of the above-mentioned "limitation". The specification does not provide sufficient support for a method of treating "B-cell immune disease" by administering a B-cell antibody. The specification only does not appear to disclose "B-cell immune disease". The instant claims now recite "B-cell immune disease" which is not clearly disclosed in the specification. Therefore, the claims represent a departure from the specification and claims originally filed. Applicant's reliance on generic disclosure (an immune disease) and possibly a single or limited species do not provide sufficient direction and guidance to the features currently claimed. It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679 683 (CCPA 1972) and MPEP 2163.05.

Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02, 2163.05-06 and 2173.05 (i).

11. Claims 78-86, 93-101, and newly added claims 102, 103 (added on December 26, 2007) and claims 104-108 (added on February 4, 2008) are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

Applicant's arguments in conjunction with the Foon declaration under 37 C.F.R. 1.132 and the references cited have been fully considered but have not been found persuasive.

In contrast to applicant's reliance on method of treating systemic lupus erythematousus or primary SjÖgren's syndrome using anti-CD22 antibody taught by Dorner et al. (Arthritis Res. Ther. 2006. 8;3:pages 1-11 (renumbered)) or Steinfeld et al. (Expert Opin. Biol. Ther. 2006. 6;9:943-9) and method of treating rheumatoid arthritis by companies such as Wyeth and Genentech, it is noted that applicant has not provided any nexus between the prior art diseases systemic lupus erythematousus, primary SjÖgren's syndrome, and rheumatoid arthritis and the instant specification.

Furthermore, the species of anti-CD22 antibody and anti-CD20 antibody are not commensurate with the scope of the claimed genus of B-cell antibody and the species of systemic lupus erythematousus, primary SjÖgren's syndrome, and rheumatoid arthritis are not commensurate with scope of the claimed genus of "an immune disease".

Moreover, as applicant admits on her own Remarks, filed on December 26, 2007, that not all antibodies that bind to B-cell can be used to treat immune diseases, only those antibodies that bind antigens well expressed on normal B cells would be effective in treating immune diseases (e.g. see paragraphs 5 and 6 on page 11 of the Remarks filed on December 26, 2007). Yet the instant claims recite any B-cell antibody or fragment thereof without considering the level of antigens that is expressed on normal B cells. Thus, one of skill in the art would not be able to

make and use the claimed invention of a method of treating immune diseases using any B-cell antibodies.

Therefore, applicant's arguments have not been found persuasive and the rejection has been maintained for reasons of record.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 78, 80-86, 97, 98, and newly added claims 102-105, 107, and 108 are rejected under 35 U.S.C. 102(b) as being anticipated by Meyer et al. (US Patent 4,861,579) for reasons of record.

Applicant's arguments in conjunction with the cited references have been fully considered but have not been found persuasive.

Applicant argues that Meyer et al. only teach Lym-1 and Lym-2 antibodies that are anti-HLA-DR antibodies. Applicant further asserts that the reference Wurflein et al. show Lym-1 and Lym-2 antibody would bind HLA class II antigen more preferentially in malignant human B cells than normal B cells and monocytes. Furthermore, applicant asserts that Epstein et al. teach that HLA-DR expression level on normal cells is low. Moreover, applicant argues that the species of B-cell antibody disclosed in the instant specification EPB2 is well expressed on normal B cell.

This is not found persuasive for following reasons:

In contrast to applicant's reliance on specific examples of Lym-1 and Lym-2 antibodies taught by Meyer et al., it is noted that the teachings of Meyer et al. are not limited to the two

examples of Lym-1 and Lym-2. A prior art reference must be considered in its entirety, MPEP 2141.02. In this case, Meyer et al. teach a method of treating immune diseases such as infection, autoimmune disease by administering an anti-B antibody or fragment thereof (see entire document, particularly columns 1-3). Therefore, the Meyer et al. method would read onto the claimed method. Even if one only considers the examples of Meyer et al. in method of treating immune diseases using Lym-1 and Lym-2 antibodies, the referenced methods using species of the B-cell antibody Lym-1 and Lym-2 would still anticipate the claimed method using genus of B-cell antibody.

Further, contrary to applicant's argument regarding limitations not claimed, it is noted that the teachings of Wurflein et al. and Epstein et al. have no nexus to the instant specification in that there is no disclosure in the instant specification indicating that the claimed B-cell antibody must have binding to antigen well expressed on normal B cell.

Furthermore, in contrast to applicant's argument that Meyer et al. does not provide written description to show Meyer et al. is in possession of the method of treating autoimmune disease with B-cell antibodies, it is noted that issued US Patents are presumed valid and enabled. Additionally, applicant is reminded that the instant specification only provide one species of LL2 antibody to support the entire genus of the claimed B-cell antibody. As such, applicant appears to argue for a double standard, holding the teachings of the prior art to a higher level under 35 U.S.C. 112, first paragraph than what is found in the instant specification.

Therefore, applicant's arguments have not been found persuasive.

16. Claims 78, 79, 81, 93, 96, and newly added 102-107 are rejected under 35 U.S.C. 102(b) as being anticipated by Bussel et al. (Blood 1988 72;1:121-127) as evidenced by de Grandmont et al. (Blood 2003 101;8:3065-3073) for reasons of record.

Applicant's arguments in conjunction with the cited reference have been fully considered but have not been found persuasive.

Applicant argues that Bussel et al. do not disclose IVIG includes antibodies against B lymphocytes. While applicant admits that Grandmont et al. teach that IVIG binds CD40, applicant asserts that CD40 is expressed on monocytes, dendritic cells, endothelial cells in addition to mature B cell. Thus, applicant asserts that IVIG does not contain B-cell antibodies. Further, applicant asserts that Teeling et al. therapeutically active ingredient in IVIG is dimers interacting with Fc gamma receptors, not B-cell antibodies. Furthermore, applicant asserts that even if IVIG contains B-cell antibodies, the amount is not sufficient to meet the claimed "therapeutically effective amount" of B-cell antibody. Thus, applicant argues the reference teachings do not anticipate the claimed invention.

This is not found persuasive for following reasons:

In contrast to applicant's reliance on the mechanism of action of IVIG, it is noted that the mechanism of action disclosed by the prior art does not preclude that the methods and compositions of the prior art IVIG inherently would have had the properties of B-cell antibody recited in the claims because compositions comprising the same type of B-cell antibodies are administered to the same patients to treat the same type of autoimmune disease ITP to achieve the same result.

Additionally, given that Grandmont et al. teach IVIG binds CD40 that is expressed on B-cell, IVIG would be considered to have B-cell antibody. Regarding applicant's argument that CD40 is also expressed on cell types other than B-cell, it is noted that during patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification." See MPEP 2111. In this case, given that no clear definition was given regarding the broadly claimed B-cell antibody as well as applicant's assertion that B-cell antibody meant antibodies targeting B cell antigens (see Interview summary mailed on December 6, 2007), IVIG containing antibodies that bind CD40 expressed on mature B cells is considered B-cell antibody. Further, regarding applicant's arguments of "therapeutically effective amount", it is noted that

the term is not defined in the instant specification. Thus, the prior art method of treating ITP with the amount of IVIG to relief the symptoms is considered "therapeutically effective amount".

Therefore, applicant's arguments have not been found persuasive.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 78, 80, 82-86, 93, 95-101, and newly added claims 104, and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meyer et al. (US Patent 4,861,579) in view of Sivam et al. (US Patent 5,116,944) for reasons of record.

Applicant's arguments in conjunction with the declarations by Dorner and Foon and references cited have been fully considered but have not been found persuasive.

Applicant's arguments and the Examiner's rebuttals regarding the teachings of Meyer et al. are essentially the same as above.

Further, applicant argues that Sivam et al. does not overcome Meyer's failure to teach treatment of an immune disease with B-cell antibody. Thus, applicant asserts that the prior art teachings do not render the instant claims obvious.

This is not found persuasive for following reasons:

In response to applicant's arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combination of references. See MPEP 2145.

It is noted that in considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom In re Preda, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968). See MPEP 2144.01.

Furthermore, specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Corp. v. Electro Materials Corp. of America 202 USPQ 22 (DC SNY); and In re Burckel 201 USPQ 67 (CCPA). In re Burckel is cited in MPEP 716.02.

Here, given the teachings of Meyer et al. regarding method of treating an immune disease using anti-B cell antibody, and the teachings of Sivam et al providing methods of making and using antibody and its fragment conjugated with cytokines, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success of practicing the claimed method of treating an immune disease by using anti-B cell antibody and its fragments that are conjugated to cytokines.

Therefore, applicant's arguments have not been found persuasive.

19. Claims 78, and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meyer et al. (US Patent 4,861,579) in view of Fishwild et al. (Nature Biotech. 1996, 14:845-851) for reasons of record.

Applicant's arguments in conjunction with the declarations by Dorner and Foon and references cited have been fully considered but have not been found persuasive.

Applicant's arguments and the Examiner's rebuttals regarding the teachings of Meyer et al. are essentially the same as above.

Further, applicant argues that Fishwild et al. does not teach treatment of an immune disease with a B-cell antibody. Thus, applicant asserts that the prior art teachings do not render the instant claims obvious.

This is not found persuasive for following reasons:

In response to applicant's arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combination of references. See MPEP 2145.

It is noted that in considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom In re Preda, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968). See MPEP 2144.01.

Furthermore, specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Corp. v. Electro Materials Corp. of America 202 USPQ 22 (DC SNY); and In re Burckel 201 USPQ 67 (CCPA). In re Burckel is cited in MPEP 716.02.

Here, given the teachings of Meyer et al. regarding method of treating an immune disease using anti-B cell antibody, and the teachings of Fishwild et al. providing methods of making and using human monoclonal antibody, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success of practicing the claimed method of treating an immune disease by using human monoclonal anti-B cell antibody.

Therefore, applicant's arguments have not been found persuasive.

20. Conclusion: no claim is allowed.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Dahle whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Eileen O'Hara can be reached 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Chun Dahle, Ph.D. (formerly Chun Crowder)
Patent Examiner
April 22, 2008

/Maher M. Haddad/
Primary Examiner,
Art Unit 1644